TUBERCULOSIS

A Guide for Practising Physicians

Revised National Tuberculosis Control Programme

Central TB Division

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Table of Contents

Introduction	1
Goal of the RNTCP	2
Transmission of Tuberculosis	3
Diagnosis	4
What is DOTS?	6
Intermittent Treatment	8
Components of DOTS	9
Role of General Practitioners	11
Services Provided by the RNTCP	13
Categories and Treatment	14
Special Situations	18
HIV and Tuberculosis	21

Introduction

Tuberculosis (TB) kills more adults in India than any other infectious disease.More than 1,000 people a day—one every minute—die of TB in our country. It is estimated that there are 14 million TB cases in our country out of which 3.5 million are sputum positive. About 1 million sputum positive cases are added every year.

India has a long history of research and demonstration projects in TB. Unfortunately, despite the existence of a National Tuberculosis Control Programme since 1962, the desired results have not been achieved. There is an overdependence on X-rays for diagnosis. Treatment regimens used are often non-standard and ineffective. In both public and private sectors, incomplete treatment is the norm rather than the exception.

On the recommendations of an expert committee, a revised strategy to control TB was pilot tested in 1993 in a population of 2.35 million and was then extended to a population of 13.85 million in 15 States/UTs in the country. In these areas, diagnostic practices improved with effective use of quality sputum microscopy, and cure rates doubled as compared to those achieved with traditional treatment. Because of these encouraging results, the Revised National Tuberculosis Control Programme (RNTCP) is being extended initially to 102 districts covering a population of 271.2 million in a phased manner.

Close cooperation between government health agencies and private practitioners is essential for the control of TB.

Goal of the RNTCP

The goal of the RNTCP is to ensure that at least 85% of all newly detected sputum-positive cases are cured and thus transmission of TB is interrupted

Transmission of Tuberculosis

When a sputum-positive pulmonary TB patient coughs or sneezes, he spreads *Mycobacterium tuberculosis* into the air in the form of tiny droplets. If a healthy person inhales these tiny particles, he may contract TB. Effective treatment of smear-positive TB patients stops TB at the source and is therefore the top priority for control of the disease.

Diagnosis

Any person with cough for more than 3 weeks should be investigated for TB. Bacteriological examination of sputum is, as a rule, the only way by which diagnosis of pulmonary TB can be confirmed. At least 3 sputum samples should be collected and examined by microscopy in a designated laboratory. High quality laboratory services are available in the RNTCP at designated microscopy centres in your area, which are established approximately for every one Lakh population. Either the sputum or the patient himself can be sent to the microscopy centre for sputum examination.

Diagnosis by X-ray is unreliable because other chest diseases often resemble TB. Judging the activity of TB by X-ray is also unreliable. Patients with abnormal lesions on chest X-ray should not be started on treatment until 3 sputum samples have been examined for AFB. Sputum microscopy not only confirms the diagnosis, but also indicates the degree of infectivity and, if positive, provides a means of monitoring response to treatment.

Smear-positive pulmonary cases: This category includes patients with at least 2 sputum samples positive for AFB by microscopy, and those with one sputum sample positive and radiological abnormalities consistent with active pulmonary TB.

Smear-negative pulmonary cases: Patients with at least 3 sputum samples negative for AFB by microscopy, radiographic abnormalities and history/clinical evidence consistent with active pulmonary TB, and decision by a

physician to treat with a **full course** of anti-tuberculosis therapy fall into this category.

Extra-pulmonary cases: These are patients with history and/or clinical evidence consistent with active TB resulting in the decision by a physician to treat with a full course of anti-tuberculosis drugs. Extra-pulmonary TB can affect any part of the body including the pleura, lymph nodes, bones and joints, genito-urinary tract, and central nervous system (meninges). Diagnosis is often difficult and may require specialized tests such as fine-needle aspiration cytology (FNAC) or biopsy. Patients with extra-pulmonary TB rarely, if ever, spread the disease to other persons.

Paediatric tuberculosis: Diagnosis of TB in children is difficult. Sputum usually cannot be obtained from them and if obtained, is often negative even on culture. Diagnosis rests largely on clinical history, history of contact with an infectious adult, X-ray examination and tuberculin testing.

All patients with cough of 3 weeks or more should have their sputum examined at RNTCP microscopy centres.

What is DOTS ?

DOTS (Directly Observed Treatment, Short-Course Chemotherapy) is a strategy to ensure cure by providing the most effective medicine and confirming that it is taken. It is the only strategy which has been documented to be effective worldwide on a programme basis. DOTS ensures that patients take medicines regularly until they are cured. During the intensive phase, a health worker or other trained person watches as the patient swallows the drugs in his presence. During the continuation phase the patient is issued medicines for one week in a multiblister combipack of which the first dose is swallowed by the patient in the presence of the health worker or other trained person. The consumption of medicines in the continuation phase is also checked by return of the empty multiblister combipack when the patient comes to collect medicine for the next week. Sputum microscopy is done at defined intervals during treatment to monitor the patient's progress toward cure.

The essential principles of DOTS were first demonstrated in India. The determination that tuberculosis patients need not be hospitalised, and the necessity and effectiveness of directly observed, intermittent treatment was first proven at the Tuberculosis Research Centre in Chennai in the 1950s and 1960s. The key to the success of the DOTS strategy is that it places the responsibility for curing TB patients on the health workers — not the patients. This strategy has proven successful

throughout the world. China has implemented DOTS for more than 650 million people, with cure rates of more than 90%. Vietnam and Cambodia have implemented highly effective programmes. And Bangladesh has now implemented DOTS in two-thirds of the country, with high cure rates and excellent collaboration with non-governmental organizations. In India the pilot projects covering a population of 13.85 million have demonstrated a cure rate of about 80%.

Intermittent Treatment

It has been proved by clinical trials that thrice-a-week, alternate-day treatment is as effective as daily treatment. The doubling time of *Mycobacteria tuberculosis* is about 18 hours, compared with 10-20 minutes for most bacteria. The tubercle bacilli do not see the sun rise and set. In animal models, intermittent treatment is *more* effective than daily treatment, presumably because intermittent dosage allows organisms to re-enter the reproductive phase, in which the bactericidal agents of isoniazid and rifampicin are more effective (Postgrad Med J 1971;47:737-741). Dozens of clinical trials have demonstrated that intermittent treatment is at least as effective as daily treatment (e.g. Tuberculosis Research Centre, Madras. Bull WHO 1964;31:247-271; Tuberculosis Research Centre, Madras. Brit Med J 1973;2:7-11; Am Rev Respir Dis 1991;143:700-706.). No differences in the number or severity of side effects has been found, although patients receiving intermittent treatment had less arthralgia in one trial (Tubercle 1976;57:81-95). However, alternate-day treatment should only be used in a programme of directly observed treatment so that it can be ensured that the patient completes the full course of treatment and is cured.

Treatment for tuberculosis is provided free of cost at all government health facilities.

Components of DOTS

The RNTCP (Revised National Tuberculosis Control Programme) is an application to India of the WHO-recommended DOTS strategy. The components of the DOTS strategy are:

➢ Diagnosis of patients who present to health facilities with cough of three weeks or more shall be done primarily by sputum microscopy using binocular microscopes and quality reagents. All the microscopists of the designated microscopy centres will be extensively trained. The system also includes multi-tier cross-checking and quality assurance of sputum smears.

➢ Regular and uninterrupted supply of drugs — drugs will be supplied directly by the manufacturers to the project sites in patientwise boxes, with sufficient buffer stocks ensured.

➢ Short-course chemotherapy given in a programme of direct observation — health workers and community volunteers will provide DOT.

➢ Systematic evaluation and monitoring. Cure rate is the main indicator of programme success.

In order to implement the RNTCP, State TB Headquarters, State Tuberculosis Training and Demonstration Centres and District Tuberculosis Centres are being strengthened. In addition, **Tuberculosis Units** (TUs) are being established at the **subdistrict** level, covering a population of approximately 5 Lakh. Each TU includes newly created posts of one **Senior Tuberculosis Supervisor** (STS) and one **Senior**

Tuberculosis Laboratory Supervisor (STLS). A designated **Medical Officer-Tuberculosis Control** (MO-TC) is responsible for all the programme activities at the TU level.

Role of General Practitioners

General practitioners are important in their community as they are trusted by patients. Physicians and others can help control TB in their community by:

- Ensuring that each and every person with productive cough for 3 weeks or more has three sputum samples examined in a designated laboratory. Two sputum samples are almost as sensitive as one culture for diagnosis;

- Using sputum microscopy as the basic tool for diagnosis and monitoring of treatment and recognizing the limited value of X-rays for diagnosis and follow-up of TB, and;

- Referring patients to RNTCP sites for diagnosis and/or treatment;

- Emphasizing to patients the critical importance of complete treatment, and that TB will be cured if complete treatment is taken;

- Emphasizing the necessity of fully observed, thrice-weekly treatment with standardized therapy in the intensive phase, and once-weekly observation in the continuation phase of treatment;

- Emphasizing the importance of screening contacts of smear-positive cases, and ensure that the symptomatic contacts are evaluated;

- Propagating the message that DOTS should be standard of

care, and is the only means to ensure cure;

- Educating the community about the signs and symptoms of TB and the need to report to designated centres if these symptoms occur;

- Educating the community at large about TB to encourage patients to complete treatment, and ensure that TB patients are not rejected by their families or others;

- In order to make services as accessible to patients as possible, government staff and private practitioners can coordinate to use the offices of private practitioners as DOTS centre;.

Services Provided by the RNTCP

The RNTCP strengthens tuberculosis control services in your area. You can be assured of:

- Free of cost services including supply of drugs to the patients;
- High quality sputum microscopy, with prompt reporting of results;
- High quality evaluation and appropriate treatment;
- High quality drugs;
- Supply of full requirements of all drugs and their uninterrupted availability;
- Provision of Direct Observation of Treatment (DOT), usually by the general health services, or by community volunteers, ensuring that drugs are actually taken by your patients;
- Technical assistance in the care of patients and control of tuberculosis.

Categories and Treatment

Category I : New cases who are sputum-positive, or seriously ill patients with smear-negative or extra-pulmonary disease.

Treatment. Treatment is given in two phases. The Intensive Phase consists of isoniazid, rifampicin, pyrazinamide and ethambutol given under direct observation thrice weekly on alternate days and lasts for 2 months (24 doses). This is immediately followed by the Continuation Phase, which consists of 4 months (18 weeks, 54 doses) of isoniazid and rifampicin given thrice weekly on alternate days, the first dose each week being directly observed. If the sputum smear is positive after 2 months of treatment, the 4 Intensive Phase drugs are continued for another one month (12 doses) before starting the 4-month Continuation Phase.

Category II : Retreatment cases including patients with relapse, failure and those who return to treatment after default. Such patients are generally sputum positive.

Treatment. Treatment is given in two phases. The Intensive Phase consists of two months (24 doses) of isoniazid, rifampicin, pyrazinamide, ethambutol and streptomycin, followed by one month of isoniazid, rifampicin, pyrazinamide, and ethambutol, all given under direct observation thrice weekly on alternate days. This is immediately followed by the Continuation Phase, which consists of 5 months (22 weeks, 66 doses) of isoniazid,rifampicin, and ethambutol

given thrice weekly on alternate days, the first dose each week being directly observed. If the sputum smear is positive after 3 months of treatment, the 4 oral Intensive Phase drugs are continued for another one month (12 doses) before starting the 5-month Continuation Phase.

Category III : Patients who are sputum-negative, or who have extra-pulmonary TB and are not seriously ill.

Treatment. Treatment is given in two phases. The Intensive Phase consists of isoniazid, rifampicin, and pyrazinamide given under direct observation thrice weekly on alternate days and lasts for 2 months (24 doses). This is immediately followed by the Continuation Phase, which consists of 4 months (18 weeks, 54 doses) of isoniazid and rifampicin given thrice weekly on alternate days, the first dose each week being directly observed. If the sputum smear is positive after 2 months of treatment, the patient is considered a treatment failure and begun afresh on Category II treatment.

Drugs are supplied in patient-wise boxes containing the full course of treatment, and packaged in blister packs. For the intensive phase, each blister pack contains one day's medication. For the continuation phase, each blister pack contains one week's supply of medication. The combipack drugs for extension of the intensive phase are supplied separately.

Dosage information is provided in the following chart:

Medication	Dose (thrice-weekly)	Number of pills in combipack
Isoniazid	600 mg	2
Rifampicin	450 mg*	1
Pyrazinamide	1500 mg	3
Ethambutol	1200 mg	3
Streptomycin**	750 mg	—

***Patients who weigh 60 kilograms or more are given an extra 150 mg dose of rifampicin.**

****Patients over 50 years of age are given 0.5 grams of streptomycin.**

SYMPTOM-BASED APPROACH TO EVALUATION OF POSSIBLE SIDE-EFFECTS OF ANTI-TUBERCULOSIS DRUGS USED IN RNTCP

Symptom	Drug (abbreviation)	Action to be taken
Drowsiness	Isoniazid (H)	Reassure patient
Red-orange urine/tears	Rifampicin (R)	Reassure patient
Gastrointestinal upset	Any oral medication	Reassure patient Give drugs with less water Give drugs over a longer period of time
Burning in the hands, feet	Isoniazid (H)	Give pyridoxine 100 mg/day until symptoms subside
Joint pains	Pyrazinamide (Z)	If severe, refer patient for evaluation
Impaired vision	Ethambutol (E)	STOP treatment, refer patient for evaluation
Ringing in the ears	Streptomycin (S)	STOP streptomycin, refer patient for evaluation
Loss of hearing	Streptomycin (S)	STOP streptomycin, refer patient for evaluation
Dizziness, loss of balance	Streptomycin (S)	STOP streptomycin, refer patient for evaluation
Jaundice	Isoniazid (H) Rifampicin (R) Pyrazinamide (Z)	STOP treatment, refer patient for evaluation

***Note*: In all cases of jaundice, anti-tuberculosis drugs should be stopped immediately and the patient referred for evaluation.**

Special Situations

Hospitalization

Generally, patients with TB do not need hospitalization. Those who are extremely ill can be hospitalized during the initial phase of treatment. In addition, all patients with significant haemoptysis, pneumothorax or large accumulation of pleural fluid leading to breathlessness, should be referred to a hospital.

Tuberculous meningitis

Tuberculous meningitis is fatal if untreated. Patients should generally be referred to the hospital. Treatment should be started as soon as possible. The patient should be put on Category I treatment, with the continuation phase lasting for 6-7 months. Steroids should be given initially to reduce meningeal inflammation and reduced gradually over 6-8 weeks.

Treatment of tuberculosis during pregnancy

Streptomycin should not be given during pregnancy; other drugs used in the RNTCP are safe during pregnancy. Breast-feeding should continue regardless of the mother's TB status.

Contacts of smear-positive index cases

Any contact person of a smear-positive case who has productive cough should have 3 sputum examinations as soon as possible for diagnosis. If sputum examinations are negative

broad-spectrum antibiotics, X-ray should be done and the patient evaluated clinically. Children who have symptoms should undergo X-ray and clinical examination. Tuberculin testing can be helpful in evaluating TB in children, but a positive tuberculin test does not confirm disease, and a negative test does not rule it out.

Child contacts who are under 5 years of age

A symptomatic child contact with a positive Mantoux test (10 mm or more) is to be treated as a case, regardless of whether or not he has been given BCG vaccination in the past. Dosages of anti-TB medication for children are given in the accompanying table.

For infants, if the mother or any other household member is smear-positive then chemoprophylaxis should be given for 3 months. After this, do a Mantoux test. If the Mantoux test is negative, stop chemoprophylaxis and give BCG. If the Mantoux test is positive continue chemoprophylaxis for a total duration of 6 months.

Chemoprophylaxis and evaluation of child contacts of sputum-positive cases should be done in consultation with a paediatrician.

Effective treatment of infectious patients with short-course chemotherapy given by direct observation protects children against all forms of TB and also improves child survival by improving the health of families. The most effective way to prevent TB is to ensure that sputum smear-positive patients are cured, and the best way to ensure cure is by giving short-course chemotherapy in a programme of direct observation.

DOSAGES FOR CHILDREN

DRUGS	DAILY REGIMEN	THRICE-WEEKLY REGIMEN
Isoniazid	5 mg/kg	10 mg/kg
Rifampicin	10 mg/kg	10 mg/kg
Pyrazinamide	25 mg/kg	35 mg/kg
Streptomycin	15 mg/kg	15 mg/kg
Ethambutol*	15 mg/kg	30 mg/kg

*** Should not be given to children below six years of age**

BCG vaccination

The Chingleput study has shown that BCG vaccination does not protect individuals from developing adult-type pulmonary TB. However, the available evidence indicates that BCG prevents serious forms of TB in children.

The present policy of the Government of India is to administer BCG at birth to newborns if they are born in an institution, and between the ages of 6 weeks and 9 months otherwise under the Expanded Programme on Immunization.

Role of Non-Governmental Organizations (NGOs)

NGOs can participate in the RNTCP by administering DOTS and referring symptomatic patients for sputum examination. Patients and the community should be informed that TB can be cured if complete treatment is taken. Good coordination and liaison between NGOs and governmental efforts will improve services to patients, increase cure rates and decrease the spread of TB.

HIV and Tuberculosis

Patients with HIV infection are much more susceptible to infections, including TB. In fact, TB is one of the most serious opportunistic infections in HIV positive cases. In patients infected with both HIV and TB, the lifetime risk of developing the disease has been estimated to be at least 60%, compared to approximately 10% in persons infected with TB who do not have HIV infection.

The diagnosis of TB in patients with HIV is more difficult than in those without HIV for three reasons:

- Direct sputum smear examination is a specific test, but is not a sensitive test for the diagnosis of tuberculosis. The sensitivity of sputum microscopy as a diagnostic tool is further reduced in HIV-infected patients. Of HIV-negative patients with pulmonary TB, 50-80% will have positive sputum smears, compared with approximately 30-50% of HIV-positive patients with pulmonary TB.

- X-ray abnormalities, which are not specific for TB in HIV-negative patients, are even more non-specific in HIV-infected patients. In HIV-infected patients, TB may be present with only minor abnormalities on chest X-ray or with abnormalities which do not look like "classic" TB. This may result in under-diagnosis of pulmonary TB.

- Patients infected with HIV have frequent pulmonary infections. Because chest x-ray is a non-specific diagnostic tool for pulmonary TB, the frequent occurrence of pulmonary infections other than TB may result in over-diagnosis of TB

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among HIV-infected patients.

Patients infected with HIV have frequent pulmonary infections. Because chest x-ray is a non-specific diagnostic tool for pulmonary TB, the frequent occurrence of pulmonary infections other than TB may result in over-diagnosis of TB among HIV-infected patients.

When patients with HIV infection have chest symptoms, they should have 3 sputum examinations for AFB. If all the three sputum examinations are negative, they should receive treatment for bacterial pneumonia, which is also common in these patients. If routine antibiotics do not relieve the symptoms, then based on the results of appropriate diagnostic studies (chest X-ray, sputum culture for mycobacteria, if available), the patient can be treated for TB.

Treatment of TB in patients with HIV infection is as effective as in TB patients without HIV. Prompt diagnosis and effective treatment using DOTS can cure TB, prevent spread of the disease and prolong the life of patients with HIV. However, **because of the risk of fatal skin reactions, thiacetazone should not be used in HIV-positive persons or in areas or groups having a high prevalence of HIV**. Proper sterilization of re-usable needles and syringes, and proper disposal of disposable needles and syringes must be ensured to prevent spread of HIV and other blood-borne diseases.

It is extremely important to ensure that all patients with TB who are in a hospital or residential facility for HIV-infected persons have an uninterrupted drug supply and are on DOTS. If these patients do not take anti-tuberculosis medications as prescribed, they may spread the disease rapidly to HIV-infected persons as well as to the non-HIV-infected population.

Profile of Revised Tuberculosis Control Programme in Your Area

State Tuberculosis Office

_____ State Tuberculosis Officer

State Tuberculosis Training and Demonstration Centre

_____ Director

District Tuberculosis Centre

_____District Tuberculosis Officer

Tuberculosis Unit

_____Medical Officer — TB Control

_____Senior Treatment Supervisor

_____Senior TB Laboratory Supervisor

Microscopy Centres: **Treatment Centres:**

DOTS Providers:

Dazel/Thomson Press